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## **Neurosurgical considerations on highly eloquent brainstem cavernomas during pregnancy**

Burkhardt, J K ; Bozinov, O ; Nürnberg, J ; Shin, B ; Woernle, C M ; Ulrich, N H ; Bertalanffy, H

**Abstract:** **OBJECTIVE:** Cerebral cavernous malformations (CCMs) and especially cavernous malformations (CMs) in highly eloquent brain areas such as brainstem CMs are rare but possible events during pregnancy. Due to the few published cases in literature clear recommendations regarding the management are rare. In this study we evaluate the proceeding decision in pregnant patients with highly eloquent brainstem CMs. **METHODS:** In our series 43 patients with CMs in highly eloquent brain areas, including 39 patients with brainstem CMs, were surgically treated by the senior author between July 2007 and July 2010. Out of these, 29 patients were female and three of them presented with a symptomatic brainstem CMs during pregnancy and were included in this study. According to our experiences and to the available literature we analyzed demographic and clinical variables to provide recommendations for the management of pregnant patients with highly eloquent brainstem CMs. **RESULTS:** Only one patient was operated during pregnancy the other two patients were surgically treated after delivery, respectively. A thorough review of the literature revealed 12 patients with brainstem cavernomas during pregnancy there of only two patients were operated during pregnancy. **CONCLUSION:** Surgical treatment during pregnancy is rarely required, but needs to be performed right away in life-threatening and rapidly progressive clinical situations. Pregnant women with CMs in highly eloquent brain areas such as brainstem CMs need to be treated in specialized centers to assess the best point of time for surgery. Our study offers a useful tool to support the proceeding decision in this rare but important situation.

DOI: <https://doi.org/10.1016/j.clineuro.2012.02.040>

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ZORA URL: <https://doi.org/10.5167/uzh-72819>

Journal Article

Accepted Version

Originally published at:

Burkhardt, J K; Bozinov, O; Nürnberg, J; Shin, B; Woernle, C M; Ulrich, N H; Bertalanffy, H (2012). Neurosurgical considerations on highly eloquent brainstem cavernomas during pregnancy. *Clinical Neurology and Neurosurgery*, 114(8):1172-1176.

DOI: <https://doi.org/10.1016/j.clineuro.2012.02.040>

# **Neurosurgical Considerations on Highly Eloquent Brainstem Cavernomas during Pregnancy**

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## **Abstract**

**Background** Cerebral cavernous malformations (CCMs) and especially highly eloquent cavernous malformations (CMs) such as brainstem CMs are rare but possible events during pregnancy. Due to the few published cases in literature clear recommendations regarding the management are rare.

**Objective** To evaluate the proceeding decision in pregnant patients with highly eloquent brainstem CMs.

**Methods** In our series 43 patients with highly eloquent CMs, including 39 patients with brainstem CMs, were surgically treated by the senior author between 07/2007 to 07/2010. Out of these, 29 patients were female and three of them presented with a symptomatic brainstem CMs during pregnancy and were included in this study. According to our experiences and to the available literature we analyzed demographic and clinical variables to provide recommendations for the management of pregnant patients with highly eloquent brainstem CMs.

**Results** Only one patient was operated during pregnancy the other two patients were surgically treated after delivery, respectively. A thorough review of the literature revealed 12 patients with brainstem cavernomas during pregnancy there of only two patients were operated during pregnancy.

**Conclusions** Surgical treatment during pregnancy is rarely required, but needs to be performed right away in life-threatening and rapidly progressive clinical situations. Pregnant women with highly eloquent CMs such as brainstem CMs need to be treated in specialized centers to assess the best point of time for surgery. Our study offers a useful tool to support the proceeding decision in this rare but important situation.

## **Running Title**

Brainstem Cavernomas during Pregnancy

## **Keywords**

brainstem cavernoma, cerebral cavernous malformation, highly eloquent cavernomas, pregnancy, neurosurgery

Highly eloquent brainstem cavernous malformations (CMs) represent lesions in one of the most critical region of the brain and are challenging for both the physician in charge of treatment and the patient.<sup>1-3</sup> This subgroup represents approximately 15% of all cerebral cavernous malformations (CCMs)<sup>4</sup> and indication for surgical resection, radiation or conservative management depends on localization of the lesion and patient symptoms<sup>4-7</sup>. In case of additional physical impact for the patient, such as pregnancy, the clinical situation is even more demanding, especially since there is a growing body of evidence that these patients have a higher risk for acute CCM bleedings<sup>8, 9</sup> or even present with a de novo CCM formation.<sup>10</sup> However, the exact mechanism for this increased CCM bleeding risk is still subject of research and may be associated with the physiological hormonal changes during pregnancy including effect of estrogen.<sup>11, 12</sup> Radiation is not advisable in this clinical scenario to protect the unborn child, but surgery or conservative management needs to be carefully discussed.<sup>13, 14</sup> Such recommendations for therapy are not easy to define since only 12 cases of brainstem CMs during pregnancy are described in literature, whereof only two patients were operated during pregnancy. On this account, we present here three more cases of symptomatic brainstem CMs during pregnancy, summarize the literature and analyze our experiences to provide recommendations for therapy.

## **Methods**

### Patients:

All 39 patients (29 women, 10 men) with highly eloquent brainstem CMs including the three pregnant women were surgically treated at the Department of Neurosurgery, University Hospital Zurich, Switzerland between 07/2007 to 07/2010. Indication for surgery was performed unrelated to this study and no gender, age or race bias was present in the selection of patients. Microsurgical removal of the brainstem CM lesions were performed by the senior author (H.B.) using intra-operative neurophysiological monitoring and neuronavigation in

accordance with institutional guidelines and after patient informed consent. For analysis, the three pregnant patients with brainstem CMs were included in this study.

#### Literature review:

A PubMed database literature search for articles in English language until October 2010 was performed and the search terms “cavernoma”, “cavernous malformation”, “brainstem”, “highly eloquent cavernoma”, “intramedullary” and “pregnancy” were used. Based on these terms case reports, review articles and original articles of interest were analysed with regard to brainstem CM cases during pregnancy.

### **Results**

#### **a) Case presentations**

##### Case 1:

A 31 year old pregnant patient with a progressive hemiparesis of her left side, disturbances in swallowing, paresthesia of the tongue, left-sided central facial paresis, progressive tiredness and headache was transferred to our hospital in her 11<sup>th</sup> week of gestation. MRI with fiber tracking revealed a right-sided ponto-mesencephalic lesion associated with acute hemorrhagic portions and an accordant displacement of the surrounded corticobulbar and corticospinal fibers. (Figure 1) The patient`s symptoms deteriorated within the initial conservative course under anti-edemic drugs during the following seven days and indication for surgery was made. Before surgery perioperative management was discussed together with the anesthesiologist and gynecologist. A lumbar drain was placed to drain cerebrospinal fluid during surgery aiming to reduce the intracranial pressure and to minimize the need of brain retraction. Abdominal ultrasound of the fetus was performed before and after surgery and we refrained from a continuous perioperative monitoring of the fetus due to the early stage of pregnancy. Surgery was performed in the 12<sup>th</sup> week of gestation with a left sided subtemporal

transtentorial approach using intra-operative neurophysiological monitoring and neuronavigation and the brainstem lesion could be successfully removed gross totally. Both mother and child were in good condition after surgery and diagnosis of brainstem CM was confirmed by histopathological examination of the tissue. After surgery the clinical symptoms of the patient improved within the following week and a healthy child was delivered in time in the 40<sup>th</sup> week of pregnancy. Two months after delivery, the patient complained of an afresh impairment of her left side, anew left-sided central facial paresis and a re-bleeding in the pontine resection cave was confirmed by MRI. A CCM remnant was found in the pontine area, more dorsal and inferior compared to the initial images. (Figure 2) Contrast T1 MRI, which was not performed during pregnancy, revealed now a large associated developmental venous anomaly (DVA). This time surgery was performed via a retrosigmoidal infratentorial supracerebellar approach to assess the pontine remnant of the CCM lesion and could be removed in total. Postoperatively, the patient's symptoms improved and one year after her second operation the patient was in good condition with only minor residuals of her left hemiparesis.

### Case 2:

In this case a 34 year old woman with a known left-sided thalamo-mesencephalic CM lesion for nearly 10 years was previously treated with radiotherapy followed by conservative treatment before her first presentation in our center. Before radiation, she was suffering from a singular generalized seizure combined with minor unspecific clinical symptoms such as headache and dizziness. Within the last year her headache progressed and a paresthesia of her right hand newly occurred as well as a low-grade paresis of the right arm was present intermittent. Rebleeding of the brainstem CM lesion was confirmed by follow up MRI. At the same time pregnancy (6<sup>th</sup> week of gestation) was ascertained and the patient was transferred to our center for further evaluation. Due to the minority of her symptoms and a complete

decline of her paresis the patient was follow up conservatively and her symptoms remained stable during the whole pregnancy. One week after delivery her paresis of the right arm reoccurred and surgery was performed successfully via a parapulvinar infratentorial supracerebellar approach. The lesion could be removed completely and the patient condition improved within the following weeks.

### Case 3:

During pregnancy of her second child, this 26 year old patient recognized in her last trimester intermittent paresthesia of her feet, burning pain of her right arm and an incomplete paresis of the right abducent nerve. MRI revealed a brainstem lesion of the right pons and based on her clinical conditions and imaging conservative treatment was recommended for the patient during pregnancy. Delivery was in time and uneventfully, but three months after delivery the patient recognized progression in diplopia and worsening of the right-sided arm pain. A new hemorrhage within the known brainstem CM lesion was confirmed by MRI and indication for surgery was made. The pontine CM was removed via a retrosigmoidal infratentorial supracerebellar approach and the postoperative course was uneventfully with a complete decline of her preoperative symptoms.

### **b) Analysis of current literature**

Studies analyzing patients with cavernous malformations of the central nervous system (CNS) during pregnancy are rare in literature. Thirty CCM cases and 4 spinal intramedullary cavernous malformations (SICM) in pregnant patients were found during a thorough literature search.<sup>11, 14-16</sup> With regards to brainstem CMs, 12 cases during pregnancy were described in literature thereof only 2 cases were operated before delivery.<sup>8, 12-14</sup> All other CCM cases were treated conservatively until delivery and indication for surgery was then reassessed, 2 of the 4 SICM cases were treated microsurgically during pregnancy.<sup>9, 17-19</sup> Indication for surgery of the

brainstem CM patients were made based on the event of a symptomatic rebleeding of the CCM lesion.<sup>12, 13</sup>

## **Discussion**

Highly eloquent brainstem CMs in pregnant women affect only a small group of our population, but is a demanding situation if it occurs. According to our experiences and with regards to the available literature we presented our present management in pregnant brainstem CM patients (Figure 3). Indication for surgery is cautiously put up during pregnancy to avoid any risk for the mother and child as well as indication for surgery depends on patient clinical condition and needs to be discussed and determined individually with the patient and family (Figure 3). Especially from the anesthesiologists point of view major physiologic changes during pregnancy must be weighed up. The most important points to consider are possible difficulties in securing the airway, which is the most common cause of anesthesia-related deaths.<sup>20</sup> Pregnant women have a higher oxygen consumption and a lower functional residual capacity which lowers the time frame for apnea during intubation additionally. Also the hemodynamic parameters of pregnant women change and complicate the perioperative management. For instance, an increase of blood volume and decrease of hematocrit takes place in this setting. Furthermore, a debate about a possible impact of anesthetic drugs on neuronal development is ongoing and needs to be carefully considered when choosing a certain anesthetic regiment.<sup>21</sup>

If a brainstem CM lesion is asymptomatic, clinically stable with minor symptoms or only slowly progressive, primarily conservative treatment with regular clinical follow-ups is appropriate. In case of a life-threatening situation or rapidly progressive clinical symptoms surgery is indicated right away. From our point of view, surgery may be delayed in patients within a late stage of pregnancy with significant clinical symptoms after delivery (see patient 2) to prevent jeopardizing mother and child. In patients with rather similar symptoms



occurring in the early stage of pregnancy surgery is indicated, since the due date is far-off and delaying surgery after pregnancy is too hazardous (Figure 3).

If surgery is indicated, surgical approach and setting need to be planned carefully together with the anesthesiologist and gynecologist to minimize operation and anesthesia time as well as to discuss perioperative management.<sup>22, 23</sup> Most notable, any manipulation of the brainstem needs to be avoided, which may lead to a dangerous clinical condition.<sup>13</sup> Surgical planning is constricted since pre-/postoperative contrast enhanced images are not advisable during pregnancy. This may lead to difficulties detecting CCM associated DVAs or the correlation between the brainstem CM lesion and brainstem supplying arteries/veins.

For instance, in our first patient we decided initially to perform a subtemporal transtentorial approach to access the CCM lesion located in the medial and upper part of the brainstem to avoid any manipulation of the posterior fossa within the brainstem. We removed the hematoma and CCM lesion gross totally without challenging a total removal through an extended approach and to danger the pregnancy. Obviously, the lesion was not removed completely since the patient suffered from a symptomatic rebleeding after delivery and the remnant of the lesion was removed via a second surgery using a retrosigmoidal infratentorial supracerebellar approach. Despite the necessity for a second operation after delivery our first management was still content. Contrast images after delivery revealed a large associated DVA in the dorsal part of the CM lesion, which would have challenged an initial approach via the posterior fossa.

With regards to the literature, one of the two surgical treated cases was described in more detail.<sup>12, 13</sup> Similar to our case, indication to surgery was based on a symptomatic rebleeding of the brainstem lesion. Flemming et al. removed the highly eloquent lesion via a suboccipital craniotomy and the patient delivered a healthy child with a significant improved clinical course after surgery.<sup>13</sup> In the largest series of 100 brainstem CMs Porter et al described 7 cases of pregnant patients, whereof one case was treated surgically.<sup>12</sup> However these cases

were not described in further detail. The rest of the 9 brainstem CM patients in literature were followed up conservatively during pregnancy.<sup>8, 13, 14</sup>

## **Conclusions**

Symptomatic highly eloquent CMs and especially brainstem CMs during pregnancy remain a rare but severe event and need to be treated in specialized neurosurgical centers if diagnosed. In case of a life-threatening situation or rapidly progressive clinical symptoms surgery during pregnancy should be performed immediately, especially in the first weeks of gestation. If a brainstem CM lesion is asymptomatic, clinically stable with minor symptoms or shows only a slowly progressive pattern, primarily conservative treatment with regular clinical follow-ups during pregnancy is appropriate and re-evaluation should be taken in account after delivery.

## **Disclosure**

This study was financially independent and any financial support was received for this study.

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## Figure Legend

Figure 1: preoperative MRI (A-C), intra-operative view (D) and postoperative MRI (E-G) of patient 1 during pregnancy: Axial (A) and sagittal (B) T2W images show a large right-sided brainstem CM lesion. Diffusion tensor imaging fiber tracking (C) detect a displacement of the right corticobulbar and corticospinal fibers. Intra-operative microscopic view shows the surgical cave after CCM removal (D).

Figure 2: preoperative MRI (A-C), intra-operative view (D) and postoperative MRI (E, F) of patient 1 after delivery: Axial (A), sagittal (B) and coronal (C) MRI planes show the remnant of the CCM lesion and a large DVA (arrow, B). Intra-operative microscopic view (D) shows the surgical cave and the cavernoma remnant (asterisk).

Figure 3: Treatment chart to support the proceeding decision in patients with highly eloquent brainstem CMs during pregnancy.